WO 2005/017190

WHAT IS CLAIMED IS:

1. A compound of Formula I:

$$(R^4)_n$$
 R^3
 R^5
 R^1
 R^{10}
 R^{10}
 R^{10}
 R^{10}
 R^{10}
 R^{10}
 R^{10}
 R^{10}
 R^{10}
 R^{10}

5 or a pharmaceutically acceptable salt or stereoisomer thereof, wherein:

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a is 0 or 1;
b is 0 or 1;
10 m is 0, 1, or 2;
n is 0, 1, 2 or 3;
r is 0 or 1;
s is 0 or 1;
t is 0, 1 or 2;
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R¹ and R² are independently selected from: H, (C₁-C₆)alkyl, aryl, heterocyclyl and (C₃-C₆)cycloalkyl, optionally substituted with one, two or three substituents selected from R⁷;

R³ is selected from:

20 1) hydrogen;
2) C₁-C₁₀ alkyl;
3) C₁-C₁₀ alkyl-O-R^d,
4) C₂-C₁₀ alkenyl-O-R^d,
5) C₂-C₁₀ alkynyl-O-R^d,
6) (C₁-C₆-alkylene)_nC₃-C₈ cycloalkyl-O-R^d,

- 7) C_1 - C_{10} alkyl- $(C=O)_b$ - NR^cR^c ,
- 8) C2-C10 alkenyl-(C=O)bNRcRc',
- 9) C2-C10 alkynyl-(C=O)bNRcRc',
- 10) (C₁-C₆-alkylene)_nC₃-C₈ cycloalkyl-(C=O)_bNR^cR^c,
- 5 11) C_1 - C_{10} alkyl- $S(O)_m$ - R^d ,
 - 12) C_2 - C_{10} alkenyl- $S(O)_m$ -Rd,
 - 13) C_2 - C_{10} alkynyl- $S(O)_m$ - R^d ,
 - 14) (C₁-C₆-alkylene)_nC₃-C₈ cycloalkyl-S(O)_m-R^d,

said alkyl, alkenyl, alkynyl and cycloalkyl are optionally substituted with one or more substituents selected from R⁶;

R4 is independently selected from:

- 1) $(C=O)_aO_bC_1-C_{10}$ alkyl,
- 2) (C=O)_aO_baryl,
- 15 3) CO₂H,
 - 4) halo,
 - 5) CN,
 - 6) OH,
 - 7) ObC1-C6 perfluoroalkyl,
- 20 8) $O_a(C=O)_bNR^8R^9$,
 - 9) $S(O)_m R^a$,
 - 10) $S(O)_2NR^8R^9$,

said alkyl, aryl, alkenyl, alkynyl, heterocyclyl, and cycloalkyl optionally substituted with one, two or three substituents selected from R⁷;

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R⁵ is selected from:

- 1) hydrogen;
- 2) $(C=O)_aO_bC_1-C_{10}$ alkyl,
- 3) $(C=O)_aO_baryl$,
- 30 4) CO₂H,
 - 5) halo,
 - 6) CN,
 - 7) OH,
 - 8) ObC1-C6 perfluoroalkyl,
- 35 9) $O_a(C=O)_bNR^8R^9$,

- 10) $S(O)_mR^a$,
- 11) $S(O)_2NR^8R^9$,

said alkyl, aryl, alkenyl, alkynyl, heterocyclyl, and cycloalkyl optionally substituted with one, two or three substituents selected from R7;

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R6 is independently selected from:

- 1) $(C=O)_aO_bC_1-C_{10}$ alkyl,
- 2) $(C=O)_aO_baryl$,
- 3) C2-C10 alkenyl,
- 10 4) C2-C₁₀ alkynyl,
 - 5) (C=O)_aO_b heterocyclyl,
 - 6) CO₂H,
 - 7) halo,
 - 8) CN,
- 15 9) OH,
 - 10) ObC1-C6 perfluoroalkyl,
 - 11) $O_a(C=O)_bNR^8R^9$,
 - 12) $S(O)_m R^a$,
 - 13) $S(O)_2NR^8R^9$,
- 20 14) oxo,
 - 15) CHO,
 - 16) $(N=0)R^8R^9$, or
 - 17) (C=O)_aO_bC₃-C₈ cycloalkyl,

said alkyl, aryl, alkenyl, alkynyl, heterocyclyl, and cycloalkyl optionally substituted with one, two or three substituents selected from R⁷;

R⁷ is selected from:

- 1) $(C=O)_rO_s(C_1-C_{10})$ alkyl,
- 2) O_r(C₁-C₃)perfluoroalkyl,
- 30 3) oxo,
 - 4) OH,
 - 5) halo,
 - 6) CN,
 - 7) (C2-C10)alkenyl,
- 35 8) (C₂-C₁₀)alkynyl,

- 9) $(C=O)_{r}O_{s}(C_{3}-C_{6})$ cycloalkyl,
- 10) $(C=O)_rO_s(C_0-C_6)$ alkylene-aryl,
- 11) $(C=O)_rO_s(C_0-C_6)$ alkylene-heterocyclyl,
- 12) $(C=O)_rO_s(C_0-C_6)$ alkylene- $N(R^b)_2$.
- 5 13) $C(O)R^a$,
 - 14) (C₀-C₆)alkylene-CO₂R^a
 - 15) C(O)H,
 - 16) (C₀-C₆)alkylene-CO₂H, and
 - 17) $C(O)N(R^b)_{2}$,
- 10 18) $S(O)_m R^a$, and
 - 19) $S(O)_2N(R^b)_2;$

said alkyl, alkenyl, alkynyl, cycloalkyl, aryl, alkylene and heterocyclyl is optionally substituted with up to three substituents selected from R^b, OH, (C₁-C₆)alkoxy, halogen, CO₂H, CN, O(C=O)C₁-C₆ alkyl, oxo, NO₂ and N(R^b)₂;

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R⁸ and R⁹ are independently selected from:

- 1) H,
- 2) $(C=O)O_bC_1-C_{10}$ alkyl,
- 3) (C=O)ObC3-C8 cycloalkyl,
- 20 4) (C=O)Obaryl,
 - 5) (C=O)Obheterocyclyl,
 - 6) C₁-C₁₀ alkyl,
 - 7) aryl,
 - 8) C_2 - C_{10} alkenyl,
- 25 9) : C₂-C₁₀ alkynyl,
 - 10) heterocyclyl,
 - 11) C3-C8 cycloalkyl,
 - 12) SO₂Ra, and
 - 13) $(C=O)NRb_{2}$

said alkyl, cycloalkyl, aryl, heterocylyl, alkenyl, and alkynyl is optionally substituted with one, two or three substituents selected from R7, or

R⁸ and R⁹ can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 3-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from R⁷;

R¹⁰ is selected from: F and -CH₂F;

R¹¹ and R¹² are independently selected from: H and -CH₂F;

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R^{ox} is absent or is oxo;

R^a is independently selected from: (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl, aryl, or heterocyclyl, optionally substituted with one, two or three substituents selected from R⁷;

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- Rb is independently selected from: H, (C₁-C₆)alkyl, aryl, heterocyclyl, (C₃-C₆)cycloalkyl, (C=O)OC₁-C₆ alkyl, (C=O)C₁-C₆ alkyl, (C=O)aryl, (C=O)heterocyclyl, (C=O)NReRe 'or S(O)₂Ra, optionally substituted with one, two or three substituents selected from R⁷:
- R^cand R^c are independently selected from: H, (C₁-C₆)alkyl, aryl, NH₂, OH, ORa, -(C₁-C₆)alkyl-OH, (C₁-C₆)alkyl-O-(C₁-C₆)alkyl, (C=O)OC₁-C₆ alkyl, (C=O)C₁-C₆ alkyl, (C=O)aryl, (C=O)heterocyclyl, (C=O)NReRe ', S(O)₂Ra and -(C₁-C₆)alkyl-N(R^b)₂, wherein the alkyl is optionally substituted with one, two or three substituents selected from R⁷; or
- R^c and R^c can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 3-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from R⁷;
- Rd is selected from: H, (C1-C6)alkyl, -(C2-C6)alkyl-OH, -(C1-C6)alkyl-O-(C1-C6)alkyl and -(C1-C6)alkyl-N(R^b)2, wherein the alkyl is optionally substituted with one, two or three substituents selected from R7;
- Re and Re' are independently selected from: H, (C₁-C₆)alkyl, aryl, heterocyclyl and (C₃-C₆)cycloalkyl, optionally substituted with one, two or three substituents selected from R⁷; or
 - Re and Re' can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 3-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from R7.

2. The compound according to Claim 1 of Formula II:

$$(R^4)_n$$
 R^3
 R^5
 R^1
 $(R^{10})_t$
 R^2
 R^{12}
 R^{12}
 R^{12}

or a pharmaceutically acceptable salt or stereoisomer thereof,

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wherein:

a is 0 or 1;
b is 0 or 1;
10 m is 0, 1, or 2;
n is 0, 1, 2 or 3;
r is 0 or 1;
s is 0 or 1;
t is 0 or 1;

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R¹ and R² are independently selected from: H, (C₁-C₆)alkyl, aryl, heterocyclyl and (C₃-C₆)cycloalkyl, optionally substituted with one, two or three substituents selected from R⁷;

R³ is selected from:

- 1) hydrogen;
- 2) C_1 - C_{10} alkyl;
- 3) C_1 - C_{10} alkyl-O- R^d ,
- 4) C2-C10 alkenyl-O-Rd,
- 5) C2-C10 alkynyl-O-Rd,

- 6) (C₁-C₆-alkylene)_nC₃-C₈ cycloalkyl-O-Rd,
- 7) C_1 - C_{10} alkyl- $(C=O)_b$ -NRCRC',
- 8) C2-C10 alkenyl-(C=O)bNRcRc',
- 9) C2-C10 alkynyl-(C=O)bNRcRc',
- 5 (C₁-C₆-alkylene)_nC₃-C₈ cycloalkyl-(C=O)_bNR^cR^c ',
 - 11) C_1 - C_{10} alkyl- $S(O)_m$ -Rd,
 - 12) C_2 - C_{10} alkenyl- $S(O)_m$ - R^d ,
 - 13) C_2 - C_{10} alkynyl- $S(O)_m$ -Rd,
 - 14) (C₁-C₆-alkylene)_nC₃-C₈ cycloalkyl-S(O)_m-Rd,
- said alkyl, alkenyl, alkynyl and cycloalkyl are optionally substituted with one or more substituents selected from R⁶;

R⁴ is independently selected from:

- 1) $(C=O)_aO_bC_1-C_{10}$ alkyl,
- 15 2) $(C=O)_aO_baryl$,
 - 3) CO₂H,
 - 4) halo,
 - 5) CN,
 - 6) OH,
- 20 7) ObC1-C6 perfluoroalkyl,
 - 8) $O_a(C=O)_bNR^8R^9$,
 - 9) $S(O)_mR^a$,
 - 10) $S(O)_2NR^8R^9$,

said alkyl, aryl, alkenyl, alkynyl, heterocyclyl, and cycloalkyl optionally substituted with one, two or three substituents selected from R⁷;

R⁵ is selected from:

- 1) hydrogen;
- 2) $(C=O)_aO_bC_1-C_{10}$ alkyl,
- 3) $(C=O)_aO_{baryl}$,
- 30 4) CO₂H,
 - 5) halo,
 - 6) CN,
 - 7) OH,
 - 8) O_bC₁-C₆ perfluoroalkyl,
- 35 9) $O_a(C=O)_bNR^8R^9$,

- 10) $S(O)_m R^a$,
- 11) $S(O)_2NR^8R^9$,

said alkyl, aryl, alkenyl, alkynyl, heterocyclyl, and cycloalkyl optionally substituted with one, two or three substituents selected from R7;

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R6 is independently selected from:

- 1) $(C=O)_aO_bC_1-C_{10}$ alkyl,
- 2) (C=O)aObaryl,
- 3) C2-C₁₀ alkenyl,
- 10 4) C2-C10 alkynyl,
 - 5) (C=O)_aO_b heterocyclyl,
 - 6) CO₂H,
 - 7) halo,
 - 8) CN,
- 15 9) OH,
 - 10) ObC1-C6 perfluoroalkyl,
 - 11) $O_a(C=O)_bNR^8R^9$,
 - 12) $S(O)_mR^a$,
 - 13) $S(O)_2NR^8R^9$,
- 20 14) oxo,
 - 15) CHO,
 - 16) $(N=O)R^8R^9$, or
 - 17) (C=O)aObC3-C8 cycloalkyl,

said alkyl, aryl, alkenyl, alkynyl, heterocyclyl, and cycloalkyl optionally substituted with one, two or three substituents selected from R⁷;

R⁷ is selected from:

- 1) $(C=O)_rO_s(C_1-C_{10})$ alkyl,
- 2) $O_r(C_1-C_3)$ perfluoroalkyl,
- 3) oxo,
- 30 4) OH,
 - 5) halo,
 - 6) CN,
 - 7) (C2-C10)alkenyl,
 - 8) (C2-C10)alkynyl,
- 35 9) $(C=O)_rO_s(C_3-C_6)$ cycloalkyl,

- 10) $(C=O)_rO_s(C_0-C_6)$ alkylene-aryl,
- 11) (C=O)_rO_s(C₀-C₆)alkylene-heterocyclyl,
- 12) $(C=O)_rO_s(C_0-C_6)$ alkylene- $N(R^b)_2$,
- 13) $C(O)R^{a}$,
- 5 (C₀-C₆)alkylene-CO₂R^a
 - 15) C(O)H,
 - 16) (C₀-C₆)alkylene-CO₂H, and
 - 17) $C(O)N(R^b)_2$,
 - 18) S(O)_mRa, and
- 10 19) $S(O)_2N(R^b)_2$;

said alkyl, alkenyl, alkynyl, cycloalkyl, aryl, alkylene and heterocyclyl is optionally substituted with up to three substituents selected from R^b, OH, (C₁-C₆)alkoxy, halogen, CO₂H, CN, O(C=O)C₁-C₆ alkyl, oxo, NO₂ and N(R^b)₂;

- 15 R⁸ and R⁹ are independently selected from:
 - 1) H,
 - 2) $(C=O)O_bC_1-C_{10}$ alkyl,
 - 3) (C=O)ObC3-C8 cycloalkyl,
 - 4) (C=O)Obaryl,
- 20 5) (C=O)Obheterocyclyl,
 - 6) C₁-C₁₀ alkyl,
 - 7) aryl,
 - 8) C2-C₁₀ alkenyl,
 - 9) C₂-C₁₀ alkynyl,
- 25 10) heterocyclyl,

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- 11) C3-C8 cycloalkyl,
- 12) SO₂R^a, and
- 13) (C=O)NRb₂,

said alkyl, cycloalkyl, aryl, heterocylyl, alkenyl, and alkynyl is optionally substituted with one, two or three substituents selected from R7, or

R⁸ and R⁹ can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 3-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from R⁷;

R¹⁰ is selected from: F and -CH₂F;

R12 is selected from: H and -CH₂F, provided that when t is 1, R12 is H;

Rox is absent or is oxo:

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R^a is independently selected from: (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl, aryl, or heterocyclyl, optionally substituted with one, two or three substituents selected from R⁷;

Rb is independently selected from: H, (C_1-C_6) alkyl, aryl, heterocyclyl, (C_3-C_6) cycloalkyl, (C=O)OC1-C6 alkyl, (C=O)aryl, (C=O)heterocyclyl, (C=O)NReRe 'or $S(O)_2$ Ra, optionally substituted with one, two or three substituents selected from R^7 ;

- Rcand Rc are independently selected from: H, (C1-C6)alkyl, aryl, NH2, OH, ORa, -(C1-C6)alkyl-OH, (C1-C6)alkyl-O-(C1-C6)alkyl, (C=O)OC1-C6 alkyl, (C=O)C1-C6 alkyl, (C=O)aryl, (C=O)heterocyclyl, (C=O)NReRe , S(O)₂Ra and -(C1-C6)alkyl-N(Rb)₂, wherein the alkyl is optionally substituted with one, two or three substituents selected from R⁷; or
- Rc and Rc' can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 3-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from R7; Rd is selected from: H, (C1-C6)alkyl, -(C2-C6)alkyl-OH, -(C1-C6)alkyl-O-(C1-C6)alkyl and -(C1-C6)alkyl-N(R^b)2, wherein the alkyl is optionally substituted with one, two or three substituents selected from R7;

Re and Re' are independently selected from: H, (C1-C6)alkyl, aryl, heterocyclyl and (C3-C6)cycloalkyl, optionally substituted with one, two or three substituents selected from R7; or

Re and Re' can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 3-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from R⁷.

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3. The compound according to Claim 2 of Formula III:

or a pharmaceutically acceptable salt or stereoisomer thereof,

5 wherein:

a is 0 or 1;

b is 0 or 1;

m is 0, 1, or 2;

10 n is 0, 1 or 2;

r is 0 or 1;

s is 0 or 1;

R¹ and R² are independently selected from: H, (C₁-C₆)alkyl, aryl and (C₃-C₆)cycloalkyl, optionally substituted with one, two or three substituents selected from R⁷;

R⁴ is independently selected from:

- 1) halo,
- 2) OH,
- 20 3) ObC₁-C₆ perfluoroalkyl,

R⁵ is selected from:

- 1) hydrogen,
- 2) halo,

- 3) OH,
- 4) ObC1-C6 perfluoroalkyl,

R⁷ is selected from:

- 5 1) $(C=O)_rO_s(C_1-C_{10})$ alkyl,
 - 2) O_r(C₁-C₃)perfluoroalkyl,
 - 3) oxo,
 - 4) OH,
 - 5) halo,
- 10 6) CN,
 - 7) (C₂-C₁₀)alkenyl,
 - 8) (C_2-C_{10}) alkynyl,
 - 9) $(C=O)_rO_s(C_3-C_6)$ cycloalkyl,
 - 10) $(C=O)_rO_s(C_0-C_6)$ alkylene-aryl,
- 15 (C=O) $_{r}O_{s}(C_{0}-C_{6})$ alkylene-heterocyclyl,
 - 12) $(C=O)_rO_s(C_0-C_6)$ alkylene- $N(R^b)_2$,
 - 13) $C(O)R^a$,
 - 14) (C₀-C₆)alkylene-CO₂R^a
 - 15) C(O)H,
- 20 (C₀-C₆)alkylene-CO₂H, and
 - 17) $C(O)N(R^b)_{2}$
 - 18) $S(O)_m R^a$, and
 - 19) S(O)2N(Rb)2;

said alkyl, alkenyl, alkynyl, cycloalkyl, aryl, alkylene and heterocyclyl is optionally substituted with up to three substituents selected from R^b, OH, (C₁-C₆)alkoxy, halogen, CO₂H, CN, O(C=O)C₁-C₆ alkyl, oxo, NO₂ and N(R^b)₂;

R⁸ and R⁹ are independently selected from:

- 1) H,
- 30 2) $(C=O)O_bC_1-C_{10}$ alkyl,
 - 3) (C=O)ObC3-C8 cycloalkyl,
 - 4) (C=O)Obaryl,
 - 5) (C=O)Obheterocyclyl,
 - 6) C₁-C₁₀ alkyl,
- 35 7) aryl,

- 8) C2-C10 alkenyl,
- 9) C2-C₁₀ alkynyl,
- 10) heterocyclyl,
- 11) C3-C8 cycloalkyl,
- 12) SO₂Ra, and

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13) $(C=O)NRb_2$,

said alkyl, cycloalkyl, aryl, heterocylyl, alkenyl, and alkynyl is optionally substituted with one, two or three substituents selected from R⁷, or

- 10 R⁸ and R⁹ can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 3-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from R⁷;
- 15 R^a is independently selected from: (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl, aryl, or heterocyclyl, optionally substituted with one, two or three substituents selected from R⁷;
 - Rb is independently selected from: H, (C₁-C₆)alkyl, aryl, heterocyclyl, (C₃-C₆)cycloalkyl, (C=O)OC₁-C₆ alkyl, (C=O)aryl, (C=O)heterocyclyl, (C=O)NReRe 'or S(O)₂Ra, optionally substituted with one, two or three substituents selected from R⁷;
 - R^cand R^c are independently selected from: H, (C₁-C₆)alkyl, aryl, NH₂, OH, OR^a, -(C₁-C₆)alkyl-OH, (C₁-C₆)alkyl-O-(C₁-C₆)alkyl, (C=O)C₁-C₆ alkyl, (C=O)C₁-C₆ alkyl, (C=O)aryl, (C=O)heterocyclyl, (C=O)NR^eR^e, S(O)₂R^a and -(C₁-C₆)alkyl-N(R^b)₂, wherein the alkyl is optionally substituted with one, two or three substituents selected from R⁷; or
 - R^c and R^c' can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 3-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from R⁷;
 - Re and Re' are independently selected from: H, (C₁-C₆)alkyl, aryl, heterocyclyl and (C₃-C₆)cycloalkyl, optionally substituted with one, two or three substituents selected from R⁷; or
- Re and Re' can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 3-7 members in each ring and optionally containing, in addition to the nitrogen,

one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from R7.

4. The compound according to Claim 3 of the formula IV:

or a pharmaceutically acceptable salt or stereoisomer thereof,

wherein:

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a is 0 or 1;

10 b is 0 or 1;

m is 0, 1, or 2;

r is 0 or 1;

s is 0 or 1;

R¹ and R² are independently selected from: H and (C₁-C₆)alkyl, optionally substituted with one, two or three substituents selected from R⁷;

R4 is independently selected from:

- 1) halo,
- 2) OH,
- 3) ObC1-C6 perfluoroalkyl,

R7 is selected from:

- 1) $(C=O)_rO_s(C_1-C_{10})$ alkyl,
- 25 2) O_r(C₁-C₃)perfluoroalkyl,

3) oxo, 4) OH, 5) halo, CN, 6) 5 7) (C2-C10)alkenyl, 8) (C2-C10)alkynyl, $(C=O)_rO_s(C_3-C_6)$ cycloalkyl, 9) 10) $(C=O)_rO_s(C_0-C_6)$ alkylene-aryl, 11) (C=O)_rO_s(C₀-C₆)alkylene-heterocyclyl, $(C=O)_TO_S(C_0-C_6)$ alkylene- $N(R^b)_2$, 10 12) $C(O)R^{a}$ 13) 14) (C₀-C₆)alkylene-CO₂R^a C(O)H15) (C₀-C₆)alkylene-CO₂H, and 16) 15 $C(O)N(R^b)_2$ 17) 18) S(O)mRa, and

said alkyl, alkenyl, alkynyl, cycloalkyl, aryl, alkylene and heterocyclyl is optionally substituted with up to three substituents selected from Rb, OH, (C1-C6)alkoxy, halogen, CO2H, CN, O(C=O)C1-C6 alkyl, oxo, NO2 and N(Rb)2;

 R^8 and R^9 are independently selected from:

 $S(O)_2N(R^b)_2;$

19)

1) 25 2) (C=O)ObC1-C10 alkyl, 3) (C=O)ObC3-C8 cycloalkyl, 4) (C=O)Obaryl, 5) (C=O)Obheterocyclyl, 6) C₁-C₁₀ alkyl, 30 7) aryl, 8) C2-C10 alkenyl, 9) C2-C10 alkynyl, 10) heterocyclyl, 11) C3-C8 cycloalkyl,

SO₂Ra, and

12)

13) $(C=O)NRb_{2}$

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said alkyl, cycloalkyl, aryl, heterocylyl, alkenyl, and alkynyl is optionally substituted with one, two or three substituents selected from R7, or

- R⁸ and R⁹ can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 3-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from R⁷;
- 10 R^a is independently selected from: (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl, aryl, or heterocyclyl, optionally substituted with one, two or three substituents selected from R⁷;

Rb is independently selected from: H, (C₁-C₆)alkyl, aryl, heterocyclyl, (C₃-C₆)cycloalkyl, (C=O)OC₁-C₆ alkyl, (C=O)aryl, (C=O)heterocyclyl, (C=O)NReRe 'or S(O)₂Ra, optionally substituted with one, two or three substituents selected from R⁷;

R^cand R^c ' are independently selected from: H, (C_1-C_6) alkyl, aryl, NH₂, OH, ORa, - (C_1-C_6) alkyl-OH, - (C_1-C_6) alkyl-O- (C_1-C_6) alkyl, (C=O)OC₁-C₆ alkyl, (C=O)C₁-C₆ alkyl, (C=O)aryl, (C=O)heterocyclyl, (C=O)NReRe', S(O)₂Ra and - (C_1-C_6) alkyl-N(Rb)₂, wherein the alkyl is optionally substituted with one, two or three substituents selected from R7; or

R^c and R^c' can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 3-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from R⁷;

Re and Re' are independently selected from: H, (C₁-C₆)alkyl, aryl, heterocyclyl and (C₃-C₆)cycloalkyl, optionally substituted with one, two or three substituents selected from R⁷; or

Re and Re' can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 3-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from R⁷.

5. A compound selected from:

(2S)-4-(2,5-Difluorophenyl)-N-[(3R,4R)-4-fluoropyrrolidin-3-yl]-2-(hydroxymethyl)N-phenyl-2,5-dihydro-1H-pyrrole-1-carboxamide

- (2S)-4-(2,5-Difluorophenyl)-N-[(3S,4S)-4-fluoropyrrolidin-3-yl]-2-(hydroxymethyl)N-phenyl-2,5-dihydro-1H-pyrrole-1-carboxamide
 - (2S)-4-(2,5-Difluorophenyl)-N-[(3R,4R)-4-fluoro-1-methylpyrrolidin-3-yl]-2-(hydroxymethyl)N-phenyl-2,5-dihydro-1H-pyrrole-1-carboxamide
- 10 (2S)-4-(2,5-Difluorophenyl)-N-[(3S,4S)-4-fluoro-1-methylpyrrolidin-3-yl]-2-(hydroxymethyl)N-phenyl-2,5-dihydro-1H-pyrrole-1-carboxamide
 - (2S)-4-(2,5-Difluorophenyl)-N-[(3S,5S)-5-(fluoromethyl)-pyrrolidin-3-yl]-2-(hydroxymethyl)-N-methyl-2-phenyl-2,5-dihydro-1H-pyrrole-1-carboxamide
 - (2S)-4-(2,5-Difluorophenyl)-N-[(3S,5S)-5-(fluoromethyl)-1-methylpyrrolidin-3-yl]-2-(hydroxymethyl)-N-methyl-2-phenyl-2,5-dihydro-1H-pyrrole-1-carboxamide
- (2S)-4-(2,5-Difluorophenyl)-N-[(3S,5R)-5-(fluoromethyl)-pyrrolidin-3-yl]-2-(hydroxymethyl)-N-methyl-20 2-phenyl-2,5-dihydro-1H-pyrrole-1-carboxamide
 - (2S)-4-(2,5-Difluorophenyl)-N-[(3S,5R)-5-(fluoromethyl)-1-methylpyrrolidin-3-yl]-2-(hydroxymethyl)-N-methyl-2-phenyl-2,5-dihydro-1H-pyrrole-1-carboxamide
- or a pharmaceutically acceptable salt or stereoisomer thereof.

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- 6. A pharmaceutical composition that is comprised of a compound in accordance with Claim 1 and a pharmaceutically acceptable carrier.
- 7. A method of using the compound according to Claim 1 for the preparation of a medicament useful in treating or preventing cancer in a mammal in need of such treatment.
 - 8. A method of using the compound according to Claim 1 for the preparation of a medicament useful in treating or preventing cancer in a mammal in need of such treatment, wherein the cancer is selected from histiocytic lymphoma, lung adenocarcinoma, small cell lung cancers, pancreatic cancer, gioblastomas and breast carcinoma.
 - 9. A method of using the compound according to Claim 1 for the preparation of a medicament useful for modulating mitotic spindle formation in a mammal in need of such treatment.